10/627920

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

Claims 1 to 29 (Canceled).

Claim 30 (Original) A pharmaceutically acceptable starch, especially for parenteral administration, preferably by way of injection, to a mammal, especially a human, which

a) has an amylopectin content in excess of 85 percent by weight, in which the molecular weight of said amylopectin has been reduced, preferably by shearing so that at least 80 percent by weight of the material lies within the range of 10-10,000 kDa,

b) has a purity of at most 50 μg amino acid nitrogen per gram dry weight of starch, preferably at most 20 μg, more preferably at most 10 μg, and most preferably at most 5 μg, amino acid nitrogen per gram dry weight of starch,

c) can be dissolved in a concentration exceeding 25 percent by weight in water.

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Claim 31 (Original) A pharmaceutically acceptable starch, especially for parenteral administration, preferably by way of injection, to a mammal, especially a human, which

a) has an amylopectin content in excess of 85 percent by weight, in which the molecular weight of said amylopectin has been reduced, preferably by shearing so that at least 80 percent by weight of the material lies within the range of 10-10000 kDa,

b) has a purity of at most 50 μg amino acid nitrogen per gram dry weight of starch, preferably at most 20 μg amino acid nitrogen, more preferably at most 10 μg, and most preferably at most 5 μg amino acid nitrogen per gram dry weight of starch,

c) lacks covalently bonded additional chemical groups of the type that occur in hydroxyethyl starch.

Claim 32 (Currently amended) A starch according to ~~any one of claims 30 and 31~~ claim 30 which exhibits the ability to gel in vitro.

Claim 33 (Original) A starch according to claim 31, which exhibits the ability to form microparticles in an emulsion system, especially a two-phase aqueous system.

Claim 34 (Original) A starch according to claim 31, which has an endotoxin content of less than 25 EU/g and contains fewer than 100 microorganisms per gram.

Claim 35 (Canceled).

Claim 36 (Original) A starch according to claim 31 in which said molecular weight of the amylopectin is within the range of 100-4000 kDa, preferably 200-1000 kDa and more preferably 300-600 kDa.

Claim 37 (Original) A starch according to claim 31 which can be dissolved in water in a concentration exceeding 30%, preferably exceeding 40%, and more preferably exceeding 45%, by weight.

Claim 38 (Original) A starch according to claim 31, which remains in solution at a temperature of at most 60°C, preferably 20-45°C, especially 30-37°C, for a period sufficiently long to allow combining with a substance that is temperature sensitive and/or unstable in organic solvents, especially a protein.

Claim 39 (Original) A starch according to claim 38, wherein said combining is performed at conditions which are able to retain the bioactivity of said substance.

Claim 40 (Original) A starch according to claim 31, which when dissolved in water solidifies at a temperature of 1-55°C, especially 4-37°C.

Claim 41 (Original) A starch according to claim 40, which solidifies when exposed to an initial temperature of 1-10°C, especially about 4°C, and subsequently to a temperature of 20-55°C, preferably 25-40°C, especially about 37°C.

Claim 42 (Original) Microparticles based on starch as a carrier for a biologically active substance, especially for parenteral administration, preferably by way of injection, to a mammal, especially a human, in which said starch is the starch as defined in claim 31. C32

Claim 43 (Original) Microparticles according to claim 42, which have a mean particle diameter in the range of 10-200 μm, preferably 20-100 μm, especially 20-80 μm.

Claim 44 (Currently amended) Microparticles according to ~~any one of~~ claim 42, which exhibit the ability to be dissolved by enzymatic action in vitro or eliminated from biological tissue in vivo.

Claim 45 (Currently amended) Microparticles according to ~~any one of~~ claim 42, in which the biologically active substance is a protein.

Claim 46 (New) A starch according to claim 31 which exhibits the ability to gel in vitro.

Claim 47 (New) A starch having a purity of at most 50 μg amino acid nitrogen per gram dry weight of starch and an endotoxin content of less than 25 EU/g and containing fewer than 100 microorganisms per gram, said starch being pharmaceutically acceptable for injection into a human being and obtainable by a process starting from starch in solid form with an amylopectin content in excess of 85 percent by weight expressed as dry weight of starch comprising the following steps:

(a) subjecting said solid starch to washing(s) under conditions such that proteins, lipids and endotoxins surface-localized on the starch as well as more sparingly soluble proteins are dissolved while the starch remains undissolved, and separating the starch from the dissolved material, said washings comprising a washing with an aqueous alkaline solution for dissolving said water-soluble proteins, lipids and endotoxins and a washing with an aqueous solvent with the ability to dissolve zein for dissolving said more sparingly soluble proteins,

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(b) causing the washed starch obtained from step (a) to dissolve in an aqueous medium,

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(c) subjecting the starch solution to a molecular weight reduction by shearing such that a molecular weight distribution is obtained in which at least 80 percent by weight of the material lies within the range of 10-10000 kDa; and

(d) removing residual water-soluble proteins from the starch by subjecting the starch solution to ion exchange chromatography, said ion exchange chromatography being performed either before or after the shearing step (c) wherein the starch is pharmaceutically acceptable for injection into a human being.

What is claimed is:

1. A method of inhibiting migration of a leukocyte, comprising contacting a leukocyte with a fluorinated N-acetylglucosamine.

2. The method of claim 1, wherein said N-acetylglucosamine is 2-acetamido-2-deoxy-1,3,6-tri-O-acetyl-4-deoxy-4-fluoro-D-glucopyranose or 2-acetamido-2-deoxy-1,4,6-tri-O-acetyl-3-deoxy-3-fluoro-D-glucopyranose.

3. The method of claim 1, wherein said leukocyte is a lymphoid cell.

4. The method of claim 3, wherein said lymphoid cell is a T-cell.

5. The method of claim 4, wherein said T cell is a Th1 cell.

6. The method of claim 1, wherein said leukocyte is a leukemic cell.

7. The method of claim 6, wherein said leukocyte is a lymphoma.

8. The method of claim 7, wherein said lymphoma is cutaneous lymphoma.

9. The method of claim 1, wherein said N-acetylglucosamine is present at the concentration of 0.05mM to 0.5 mM.

10. A method of inhibiting cell proliferation, comprising contacting a cell with a fluorinated N-acetylglucosamine.

11. The method of claim 10, wherein said cell is a hematopoietic cell.

12. The method of claim 11, wherein said hematopoietic cell is a hematopoietic progenitor cell.

13. The method of claim 10, wherein said cell is a leukocyte.

14. The method of claim 10, wherein said leukocyte is a leukemic cell.

15. The method of claim 10, wherein said cell is further contacted with a chemotherapeutic agent.

16. The method of claim 15, wherein said chemotherapeutic agent is selected from the group consisting of daunorubicin (DNR), cytarabine (ara-C), idarubicin, thioguanine, etoposide, and mitoxantrone.

17. A method of modulating differentiation of a cell, comprising contacting the cell with a fluorinated N-acetylglucosamine.

18. The method of claim 17, wherein said cell is a hematopoietic cell.

19. The method of claim 18, wherein said hematopoietic cell is a hematopoietic progenitor cell.

20. A method of inhibiting migration of a hematopoietic cell, comprising contacting the hematopoietic cell with a fluorinated N-acetylglucosamine.

21. The method of claim 20, wherein said hematopoietic cell is a hematopoietic progenitor cell.

22. A method of decreasing an amount of HECA-452 epitope on a glycoprotein on a cell, comprising contacting the cell with a fluorinated N-acetylglucosamine.

23. The method of claim 22, wherein said glycoprotein is PSGL-1 or CD44.

24. The method of claim 22, wherein the amount of said glycoprotein on said cell in the presence of the fluorinated N-acetylglucosamine as compared to in the absence of the fluorinated N-acetylglucosamine differs by less than 10%.

25. The method of claim 22, wherein the amount of said glycoprotein on said cell in the presence of the fluorinated N-acetylglucosamine as compared to in the absence of the fluorinated N-acetylglucosamine differs by less than 5%.

26. The method of claim 22, wherein the amount of said glycoprotein on said cell in the presence of the fluorinated N-acetylglucosamine as compared to in the absence of the fluorinated N-acetylglucosamine differs by less than 1%.

27. The method of claim 22, wherein said cell is a leukocyte, a tumor cell or a hematopoietic progenitor cell.

28. A method of inhibiting inflammation of a tissue in a subject, comprising administering to the subject a composition comprising a fluorinated N-acetylglucosamine.

29. The method of claim 28, wherein said tissue is a dermal tissue.

30. The method of claim 28, wherein said inflammation is chronic inflammation.

31. The method of claim 30, wherein said chronic inflammation is DTH.

32. The method of claim 28, wherein said inflammation is acute inflammation.

33. The method of claim 28, wherein said inflammation is cutaneous inflammation

34. The method of claim 28, wherein said inflammation is psoriasis.

35. The method of claim 28, wherein said subject suffers from or is at risk of inflammatory bowel disease, colitis or Crohn's disease.

36. The method of claim 28, wherein said subject is further administered an anti-inflammatory compound.

37. The method of claim 36, wherein said anti-inflammatory compound is selected from the group consisting of aspirin, ibuprofen, naproxen sodium (Aleve), celecoxib, prednisone, prednisolone, and dexamethasone.

38. The method of claim 28, wherein said administering is prior to an inflammatory event.

39. The method of claim 28, wherein said administering is during an inflammatory event.

40. The method of claim 28, wherein said the administering is by a route selected from the group consisting of intraperitoneal, subcutaneous, nasal, intravenous, oral, topical and transdermal delivery.

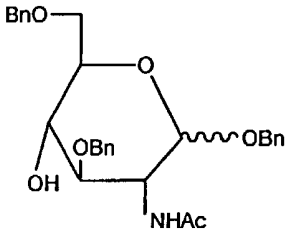
41. The method of claim 28, wherein said fluorinated N-acetylglucosamine is administered less than 50 mg/kg.

42. In a method for preparing fluorinated N-acetylglucosamine comprising the intermediate step of preparing benzyl acetamido-2-deoxy-3,6-di-O-benzyl-2-deoxy-D-glucopyranoside from benzyl 2-acetamido-3-O-benzyl-4,6-benzylidene-2-deoxy-D-glucopyranoside, the improvement comprising (i) hydrolyzing benzyl 2-acetamido-3-O-benzyl-4,6-benzylidene-2-deoxy-D-glucopyranoside under appropriate conditions to form benzyl 2-acetamido-3-O-benzyl-2-deoxy-D-glucopyranoside; (ii) reacting benzyl 2-acetamido-3-O-benzyl-2-deoxy-D-glucopyranoside with a tin compound to form a tin complex comprising benzyl 2-acetamido-3-O-benzyl-2-deoxy-D-glucopyranoside; and (iii) reacting the tin complex with a benzylating agent under appropriate conditions to form benzyl 2-acetamido-3-O-benzyl-3,6-di-O-benzyl-2-deoxy-D-glucopyranoside.

43. The method of claim 42, wherein the tin compound is bis(tributyltin)oxide.

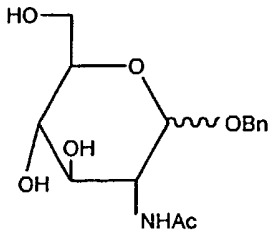
44. The method of claim 42, wherein the benzylating agent is benzyl bromide.

45. A method of making a compound having the formula (I):



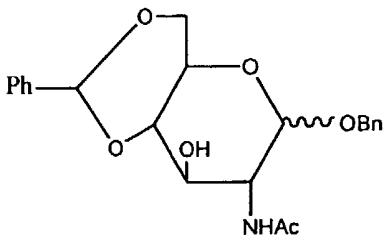
I

which comprises reacting N-acetyl-D-glucosamine with a benzylating agent under appropriate conditions to produce a compound having the formula (II):



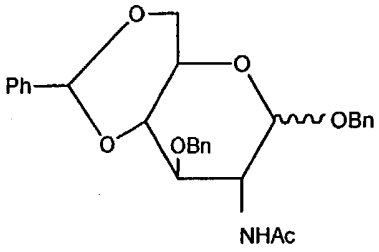
II

reacting the compound (II) with a benzaldehyde under appropriate conditions to produce a compound having the formula (III):



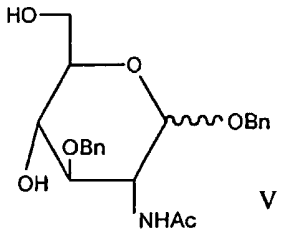
III

reacting the compound (III) with a benzylating agent under appropriate conditions to produce a compound having the formula (IV):



IV

reacting compound (IV) with a hydrolyzing agent under appropriate conditions to produce a compound having the formula (V):



V

reacting compound (V) with a tin compound to produce a tin complex comprising compound (V) and reacting the tin complex with a benzylating agent under appropriate conditions to produce compound (I).